10/535635

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<110> INCYTE CORPORATION; TRAN, Uyen K.;
      RICHARDSON, Thomas W.; BECHA, Shanya D.; ELLIOTT, Vicki S.; SWARNAKAR, Anita;
      LEE, Soo Yeun; RAMKUMAR, Jayalaxmi;
      WANG, Jonathan T.; CHIEN, David;
      MURAGE, Jaji; GERA, Mili;
      MARQUIS, Joseph P.; CHAWLA, Narinder K.;
      NAKAMURA, Lisa; KABLE, Amy E.
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<150> US 60/429,839
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<151> 2003-01-13
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Gly Ser Val Gly Gly Ala Val Thr Phe Pro Leu Lys Ser Lys Val
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Lys Gln Val Asp Ser Ile Val Trp Thr Phe Asn Thr Thr Pro Leu
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Val Thr Ile Gln Pro Glu Gly Gly Thr Ile Ile Val Thr Gln Asn
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Arg Asn Arg Glu Arg Val Asp Phe Pro Asp Gly Gly Tyr Ser Leu
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Gly Ile Tyr Ser Ser Ser Leu Gln Gln Pro Ser Thr Gln Glu Tyr
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Val Leu His Val Tyr Glu His Leu Ser Lys Pro Lys Val Thr Met
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Gly Leu Gln Ser Asn Lys Asn Gly Thr Cys Val Thr Asn Leu Thr
                                                           150
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                                      145
Cys Cys Met Glu His Gly Glu Glu Asp Val Ile Tyr Thr Trp Lys
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155

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Ala Leu Gly Gln Ala Ala Asn Glu Ser His Asn Gly Ser Ile Leu
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Pro Ile Ser Trp Arg Trp Gly Glu Ser Asp Met Thr Phe Ile Cys
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Val Ala Arg Asn Pro Val Ser Arg Asn Phe Ser Ser Pro Ile Leu
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Ala Arg Lys Leu Cys Glu Glu Asn Asn Pro Lys Gly Arg Ser Ser
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Lys Tyr Gly Leu Leu His Cys Gly Asn Thr Glu Lys Asp Gly Lys
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His Leu Gly Lys Gly His Tyr Ser Phe Tyr Ser Met Asp Ile Arg
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Glu Phe Gln Leu Pro Ser Ser Gln Ile Ser Met Val Pro Asn Val
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Gly Leu Lys Phe Ser Ile Ser Asn Ala Asn Ile Lys Ile Ser Gly
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Lys Trp Lys Ala Gln Lys Arg Phe Leu Trp Leu Ile Gln Leu Phe
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His Lys Lys Ile Glu Ser Ala Leu Arg Asn Lys Met Asn Ser Gln
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Val Cys Glu Lys Val Thr Asn Ser Val Ser Ser Lys Leu Gln Pro
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Tyr Phe Gln Thr Leu Pro Val Met Thr Lys Ile Asp Ser Val Ala
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Gly Ile Asn Tyr Gly Leu Val Ala Pro Pro Ala Thr Thr Ala Glu
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Thr Leu Asp Val Gln Met Lys Gly Glu Phe Tyr Ser Glu Asn His
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His Asn Pro Pro Pro Phe Ala Pro Pro Val Met Glu Phe Pro Ala
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Ala His Asp Arg Met Val Tyr Leu Gly Leu Ser Asp Tyr Phe Phe
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Asn Thr Ala Gly Leu Val Tyr Gln Glu Ala Gly Val Leu Lys Met
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Thr Leu Arg Asp Asp Met Ile Pro Lys Glu Ser Lys Phe Arg Leu
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Thr Thr Lys Phe Phe Gly Thr Phe Leu Pro Glu Val Ala Lys Lys
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Pro His Leu Ser Val Gln Pro Thr Gly Leu Thr Phe Tyr Pro Ala
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Val Asp Val Gln Ala Phe Ala Val Leu Pro Asn Ser Ser Leu Ala
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                                    325
Ser Leu Phe Leu Ile Gly Met His Thr Thr Gly Ser Met Glu Val
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Ser Ala Glu Ser Asn Arg Leu Val Gly Glu Leu Lys Leu Asp Arg
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Leu Leu Leu Glu Leu Lys His Ser Asn Ile Gly Pro Phe Pro Val
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                                     370
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Glu Leu Leu Gln Asp Ile Met Asn Tyr Ile Val Pro Ile Leu Val
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Leu Pro Arg Val Asn Glu Lys Leu Gln Lys Gly Phe Pro Leu Pro
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Glu Gly Thr Pro Asp Thr Val Tyr Ser Ile Glu Tyr Lys Thr Tyr
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Gly Glu Arg Asp Trp Val Ala Lys Lys Gly Cys Gln Arg Ile Thr
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                                      70
Arg Lys Ser Cys Asn Leu Thr Val Glu Thr Gly Asn Leu Thr Glu
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                                      85
Leu Tyr Tyr Ala Arg Val Thr Ala Val Ser Ala Gly Gly Arg Ser
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                                     100
                                                          105
Ala Thr Lys Met Thr Asp Arg Phe Ser Ser Leu Gln His Arg Arg
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Gln Ser Tyr Pro Gln Ala Thr
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Ala	Val	Asn	Pro	20 Gly 35	Val	Val	Val	Arg	25 Ile 40	Ser	Gln	Lys	Gly	
Asp	Tyr	Ala	Ser		G1n	Gly	Thr	Ala		Leu	Gln	Lys	Glu	
Lys	Arg	Ile	Lys	-	Pro	Asp	Tyr	Ser		Ser	Phe	Lys	Ile	
His	Leu	Gly	Lys	Gly 80	His	Tyr	Ser	Phe	Tyr 85	Ser	Met	Asp	Ile	Arg 90
Glu	Phe	Gln	Leu	Pro 95	Ser	Ser	Gln	Ile	Ser 100	Met	Val	Pro	Asn	Val 105
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_				140			Ser		145					150
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				335			Thr		340					345
Pro	Thr	Gly	Leu	350 Thr		туr	'Pro	Ala	355 Val		Val	Gln	Ala	360 Phe
Ala	Val	Leu	Pro		Ser	Ser	Leu	Ala			Phe	Leu	Ile	
Met	Val	Glu	Leu			Asp	Ile	Met			Ile	Val	Pro	
Leu	Val	Leu	Pro		Val	Asn	Glu	Lys		Gln	Lys	Gly	Phe	
Leu	Pro	Thr	Pro	410 Ala 425	Arg	Val	Gln	Leu	415 Tyr 430	Asn	Va1	Val	Leu	420 Gln 435
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                                      40
Glu Gly Thr Pro Asp Thr Val Tyr Ser Ile Glu Tyr Lys Thr Lys
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Arg Pro Gln Gly Ser Ala Gly Pro Leu Gln Cys Tyr Gly Val Gly
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Leu Leu Gly Gly Gly Val Ser Val Glu Asp Cys Cys Leu Asn Thr
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Ala Phe Ala Tyr Gln Lys Arg Ser Gly Gly Leu Cys Gln Pro Cys
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70
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Ser Pro Tyr Leu Cys Leu Leu Arg Thr Trp Cys Trp Pro Cys Gln
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Leu Cys Phe Thr Gln Tyr Glu Glu Ser Ser Gly Lys Cys Lys Gly
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Leu Leu Gly Gly Val Ser Val Glu Asp Cys Cys Leu Asn Thr
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Ala Phe Ala Tyr Gln Lys Arg Ser Gly Gly Leu Cys Gln Pro Cys
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Arg Ser Pro Arg Trp Ser Leu Trp Ser Thr Trp Ala Pro Cys Ser
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Val Thr Cys Ser Glu Gly Ser Gln Leu Arg Tyr Arg Arg Cys Val
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                 95
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Gly Trp Asn Gly Gln Cys Ser Gly Lys Val Ala Pro Gly Thr Leu
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Glu Trp Gln Leu Gln Ala Cys Glu Asp Gln Gln Cys Cys Pro Glu
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Thr Cys Ser Lys Gly Thr Arg Thr Arg Arg Arg Ala Cys Asn His
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Pro Ala Pro Lys Cys Gly Ala His Cys Pro Gly Gln Ala Gln Glu
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Ser Glu Ala Cys Asp Thr Gln Gln Val Cys Pro Thr His Gly Ala
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Trp Ala Thr Trp Gly Pro Trp Thr Pro Cys Ser Ala Ser Cys His
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Gly Gly Pro His Glu Pro Lys Glu Thr Arg Ser Arg Lys Cys Ser
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Ala Pro Glu Pro Ser Gln Lys Pro Pro Gly Lys Pro Cys Pro Gly
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Leu Ala Tyr Glu Gln Arg Arg Cys Thr Gly Leu Pro Pro Cys Pro
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                                                         255
                245
Val Asp Gly Glu Trp Asp Ser Trp Gly Glu Trp Ser Pro Cys Ile
                260
                                     265
                                                         270
Arg Arg Asn Met Lys Ser Ile Ser Cys Gln Glu Ile Pro Gly Gln
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Gln Ser Arg Gly Arg Thr Cys Arg Gly Arg Lys Phe Asp Gly His
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                290
Arg Cys Ala Gly Gln Gln Asp Ile Arg His Cys Tyr Ser Ile
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                305
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Gln His Cys Pro Leu Lys Gly Ser Trp Ser Glu Trp Ser Thr Trp

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Gly Leu Cys Met Pro Pro Cys Gly Pro Asn Pro Thr Arg Ala Arg
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Gln Arg Leu Cys Thr Pro Leu Leu Pro Lys Tyr Pro Pro Thr Val
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Ser Met Val Glu Gly Gln Gly Glu Lys Asn Val Thr Phe Trp Gly
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                                     370
                                                         375
Arg Pro Leu Pro Arg Cys Glu Glu Leu Gln Gly Gln Lys Leu Val
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                                      25
Gln Gln Ile Tyr Gly Val Val Tyr Gly Asn Val Thr Phe His Val
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                                      40
                                                           45
Pro Ser Asn Val Pro Leu Lys Glu Val Leu Trp Lys Lys Gln Lys
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Asp Lys Val Ala Glu Leu Glu Asn Ser Glu Phe Arg Ala Phe Ser
                                      70
                 65
Ser Phe Lys Asn Arg Val Tyr Leu Asp Thr Val Ser Gly Ser Leu
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                                      85
Thr Ile Tyr Asn Leu Thr Ser Ser Asp Glu Asp Glu Tyr Glu Met
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                                     100
Glu Ser Pro Asn Ile Thr Asp Thr Met Lys Phe Phe Leu Tyr Val
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                                     115
                                                          120
Leu Glu Ser Leu Pro Ser Pro Thr Leu Thr Cys Ala Leu Thr Asn
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Gly Ser Ile Glu Val Gln Cys Met Ile Pro Glu His Tyr Asn Ser
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                                     145
His Arg Gly Leu Ile Met Tyr Ser Trp Asp Cys Pro Met Glu Gln
                                     160
                155
Cys Lys Arg His Ser Arg His Arg Tyr Ala Leu Ile Pro Ile Pro
                 170
                                     175
                                                          180
Leu Ala Val Ile Thr Thr Cys Ile Val Leu Tyr Met Asn Gly Ile
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Leu Lys Cys Asp Arg Lys Pro Asp Arg Thr Asn Ser Asn
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Ile Pro Val Phe Cys Lys Ala Thr His Val Ala Gln Pro Ala Val
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Val Leu Ala Ser Ser Arg Gly Ile Ala Ser Phe Val Cys Glu Tyr
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                                      55
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Ala Ser Pro Gly Lys Ala Thr Glu Val Arg Val Thr Val Leu Arg
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                  65
Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala Ala Thr Tyr Met
                                      85
                  80
Met Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser Ile Cys Thr Gly
                                                          105
                                     100
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Thr Ser Ser Gly Asn Gln Val Asn Leu Thr Ile Gln Gly Leu Arg
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                 110
Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu Leu Met Tyr
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                 125
Pro Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln Ile Tyr
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Val Ile Ala Lys Glu Lys Lys Pro Ser Tyr Asn Arg Gly Leu Cys
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Glu Asn Ala Pro Asn Arg Ala Arg Met
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 Ala Val Ile Leu Ser Ile Leu Leu Ser Lys Gly Ser Gly Thr Gln
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 Ala Gln Leu Gln Thr Thr Arg Ala Glu Leu Gly Glu Ala Gln Ala
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Lys Leu Met Glu Gln Glu Ser Ala Leu Arg Glu Leu Arg Glu Arg
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Val Thr Gln Gly Leu Ala Glu Ala Gly Arg Gly Arg Glu Asp Val
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Arg Thr Glu Leu Phe Arg Ala Leu Glu Ala Val Arg Leu Gln Asn
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Asn Ser Cys Glu Pro Cys Pro Thr Ser Trp Leu Ser Phe Glu Gly
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                                                         135
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Ser Cys Tyr Phe Phe Ser Val Pro Lys Thr Thr Trp Ala Ala Ala
                                     145
                                                         150
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Gln Asp His Cys Ala Asp Ala Ser Ala His Leu Val Ile Val Gly
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                155
Gly Leu Asp Glu Gln Gly Phe Leu Thr Arg Asn Thr Arg Gly Arg
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                                                          180
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Gly Tyr Trp Leu Gly Leu Arg Ala Val Arg His Leu Gly Lys Val
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                185
                                     190
Gln Gly Tyr Gln Trp Val Asp Gly Val Ser Leu Ser Phe Ser His
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                                     205
Trp Asn Gln Gly Glu Pro Asn Asp Ala Trp Gly Arg Glu Asn Cys
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Leu Gly Tyr Leu Tyr Leu Gln Trp Gln Pro Pro Leu Ser Leu Asp
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His Phe Lys Glu Cys Thr Val Glu Tyr Glu Leu Lys Tyr Arg Asn
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 Ile Gly Ser Glu Thr Trp Lys Thr Ile Ile Thr Lys Asn Leu His
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                  80
 Tyr Lys Asp Gly Phe Asp Leu Asn Lys Gly Ile Glu Ala Lys Ile
                                     100
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 His Thr Leu Leu Pro Trp Gln Cys Thr Asn Gly Ser Glu Val Gln
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                 110
 Ser Ser Trp Ala Glu Thr Thr Tyr Trp Ile Ser Pro Gln Gly Ile
                                                          135
                 125
                                     130
 Pro Glu Thr Lys Val Gln Asp Met Asp Cys Val Tyr Tyr Asn Trp
                                      145
                                                          150
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 Gln Tyr Leu Leu Cys Ser Trp Lys Pro Gly Ile Gly Val Leu Leu
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 Asp Thr Asn Tyr Asn Leu Phe Tyr Trp Tyr Glu Gly Leu Asp His
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 Ala Leu Gln Cys Val Asp Tyr Ile Lys Ala Asp Gly Gln Asn Ile
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                                      190
                 185
 Gly Cys Arg Phe Pro Tyr Leu Glu Ala Ser Asp Tyr Lys Asp Phe
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                 200
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Tyr Ile Cys Val Asn Gly Ser Ser Glu Asn Lys Pro Ile Arg Ser
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Ser Tyr Phe Thr Phe Gln Leu Gln Asn Ile Val Lys Pro Leu Pro
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                                                         240
                230
Pro Val Tyr Leu Thr Phe Thr Arg Glu Ser Ser Cys Glu Ile Lys
                                                         255
                245
                                    250
Leu Lys Trp Ser Ile Pro Leu Gly Pro Ile Pro Ala Arg Cys Phe
                                                         270
                                    265
                260
Asp Tyr Glu Ile Glu Ile Arg Glu Asp Asp Thr Thr Leu Val Val
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Lys Thr Tyr Arg Arg Lys Leu Cys Tyr Val Ser Gly Tyr His Leu
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                                      40
Trp Pro Val Gln Ala Val Arg Trp Glu Lys Ile Gln Pro Arg Gln
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Thr Ser Lys Phe Pro Arg Gln Ile Val Ser Asn Cys Ser His Gly
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Arg Trp Ser Val Ile Val Ile Pro Asp Val Thr Val Ser Asp Ser
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Gly Leu Tyr Arg Cys Tyr Leu Gln Ala Ser Ala Gly Glu Asn Glu
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Thr Phe Val Met Arg Leu Thr Val Ala Glu Gly Lys Thr Asp Asn
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Gln Tyr Thr Leu Phe Val Ala Gly Gly Thr Val Leu Leu Leu
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Phe Val Ile Ser Ile Thr Thr Ile Ile Val Ile Phe Leu Asn Arg
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Arg Arg Arg Glu Arg Arg Asp Leu Phe Thr Glu Ser Trp Asp
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Thr Gln Lys Ala Pro Asn Asn Tyr Arg Ser Pro Ile Ser Thr Gly
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Gln Pro Thr Asn Gln Ser Met Asp Asp Thr Arg Glu Asp Ile Tyr
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Gly Ser Val Gly Gly Ala Val Thr Phe Pro Leu Lys Ser Lys Val
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Lys Gln Val Asp Ser Ile Val Trp Thr Phe Asn Thr Thr Pro Leu
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Val Thr Ile Gln Pro Glu Gly Gly Thr Ile Ile Val Thr Gln Asn
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Arg Asn Arg Glu Arg Val Asp Phe Pro Asp Gly Gly Tyr Ser Leu
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Lys Leu Ser Lys Leu Lys Lys Asn Asp Ser Gly Ile Tyr Tyr Val
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Gly Ile Tyr Ser Ser Ser Leu Gln Gln Pro Ser Thr Gln Glu Tyr
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                                     115
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Val Leu His Val Tyr Glu Asn Asn Pro Lys Gly Arg Ser Ser Lys
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                                     130
                 125
Tyr Gly Leu Leu His Cys Gly Asn Thr Glu Lys Asp Gly Lys Ser
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                                     145
                 140
Pro Leu Thr Ala His Asp Ala Arg His Thr Lys Ala Ile Cys Leu
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<223> Incyte ID No: 7522003CD1

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Asn Thr His Val Arg Glu Leu Thr Leu Ala Ser Ile Asp Leu Gln
                200
                                    205
Asn Thr Thr Lys Arg Pro Val Thr Thr Thr Lys Arg Glu Val Asn
                215
                                     220
Ser Ala Ile
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Met Pro Glu Glu Gly Ser Gly Cys Ser Val Arg Arg Pro Tyr
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Gly Cys Val Leu Arg Ala Ala Leu Val Pro Leu Val Ala Gly Leu
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Val Ile Cys Leu Val Val Cys Ile Gln Arg Phe Ala Gln Ala Gln
                 35
                                      40
Gln Gln Leu Pro Leu Glu Ser Leu Gly Asp Leu Ser Arg Thr Pro
                 50
                                      55
Gly Tyr Thr Gly Arg Gly Ala Gln His Trp Ala Ala Pro Ser Cys
                                      70
                                                           75
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Met Asp Gln Ser Trp Thr Arg Gly Ser Tyr Val Ser Ile Val Met
                                      85
                 80
Ala Ser Thr Trp Tyr Thr Ser Arg
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Ala Gln Thr Ile His Thr Gln Glu Glu Asp Leu Pro Arg Pro Ser
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Ile Ser Ala Glu Pro Gly Thr Val Ile Pro Leu Gly Ser His Val
                 35
                                      40
Thr Phe Val Cys Arg Gly Pro Val Gly Val Gln Thr Phe Arg Leu
                                      55
                 50
Glu Arg Glu Ser Arg Ser Thr Tyr Asn Asp Thr Glu Asp Val Ser
                 65
                                      70
Gln Ala Ser Pro Ser Glu Ser Glu Ala Arg Phe Arg Ile Asp Ser
                                      85
Lys Pro Leu Glu Ala Arg Thr Pro Arg Thr Gln Ser Pro Ala Pro
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                                     100
Gln Leu Gly Leu Cys Gln Ala Leu Lys Pro Pro Asp Leu Met His
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His Glu
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Glu Met Leu Phe Leu Ala Leu Leu Leu Pro Val Val Val Ala
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Phe Ala Arg Gly Glu Ser Arg Asn Gln Ala Gly Arg Ala Ser Ser
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Gly Glu Gly Glu Ser Gly Lys Pro Trp Gly Trp Gly Gly Ile Leu
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Met Arg Gly Leu Gly Leu Trp Leu Leu Gly Ala Met Met Leu Pro
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Ala Ile Ala Pro Ser Arg Pro Trp Ala Leu Met Glu Gln Tyr Glu
                                      25
                 20
Val Val Leu Pro Arg Arg Leu Pro Gly Pro Arg Val Arg Arg Ala
                                      40
                 35
Leu Pro Ser His Leu Gly Leu Arg Pro Glu Arg Val Ser Tyr Val
                 50
                                      55
Leu Gly Ala Thr Gly His Asn Phe Thr Leu His Leu Arg Lys Asn
                                      70
                 65
Arg Asp Leu Leu Gly Ser Gly Tyr Thr Glu Thr Tyr Thr Ala Ala
                                                          90
                                      85
                  80
Asn Gly Ser Glu Val Thr Glu Gln Pro Arg Gly Gln Asp His Cys
                                     100
                  95
Phe Tyr Gln Gly His Val Glu Gly Tyr Pro Asp Ser Ala Ala Ser
                 110
                                     115
Leu Ser Thr Cys Ala Gly Leu Arg Trp Arg Gly Arg Thr Ala Arg
                                     130
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Arg Val Pro Gly
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Gly Thr Ser Glu Ser Leu Leu Asp Asn Leu Gly Asn Asp Leu Ser
                  20
                                      25
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Asn Val Val Asp Lys Leu Glu Pro Val Leu His Glu Gly Leu Glu
                 35
                                      40
Thr Val Asp Asn Thr Leu Lys Gly Ile Leu Glu Lys Leu Lys Val
                                      55
                 50
Asp Leu Gly Val Leu Gln Lys Ser Ser Ala Trp Gln Leu Ala Lys
                 65
                                      70
Gln Lys Ala Gln Glu Ala Glu Lys Leu Leu Asn Asn Val Ile Ser
                                                          90
                 80
                                      85
Lys Leu Leu Pro Thr Asn Thr Asp Ile Phe Gly Pro Ile Ile Gly
                 95
                                     100
Gln Ile Ile Asn Leu Lys Ala Ser Leu Asp Leu Leu Thr Ala Val
                110
                                     115
Thr Ile Glu Thr Asp Pro Gln Thr His Gln Pro Val Ala Val Leu
                                                          135
                125
                                     130
Gly Glu Cys Ala Ser Asp Pro Thr Ser Ile Ser Leu Ser Leu Leu
                                     145
                140
Asp Lys His Ser Gln Ile Ile Asn Lys Phe Val Asn Ser Val Ile
                155
                                     160
Asn Thr Leu Lys Ser Thr Val Ser Ser Leu Leu Gln Lys Glu Ile
                                     175
                170
Cys Pro Leu Ile Arg Ile Phe Ile His Ser Leu Asp Val Asn Val
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                                     190
Ile Gln Gln Val Val Asp Asn Pro Gln His Lys Thr Gln Leu Gln
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Thr Leu Ile
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Asp Pro Leu Ser Thr Pro Phe Asp Asn Glu Phe Tyr Asn Gly Leu

Cys Asn Arg Asp Arg Asp Gly Asn Thr Leu Thr Tyr Tyr Arg Arg

160

175

190

180

195

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Pro Trp Asn Val Ala Ser Leu Ile Tyr Glu Glu Lys Met Phe Leu
                                    205
                200
His Val Lys Gly Glu Ile His Leu Gly Arg Phe Val Met Arg Asn
                215
                                     220
Arg Asp Val Val Leu Thr Thr Thr Phe Val Asp Asp Ile Lys Ala
                                     235
                230
Leu Pro Thr Thr Tyr Glu Lys Gly Glu Tyr Phe Ala Phe Leu Glu
                                     250
                245
Thr Tyr Gly Thr His Tyr Ser Ser Ser Gly Ser Leu Gly Gly Leu
                                                         270
                260
                                     265
Tyr Glu Leu Ile Tyr Val Leu Asp Lys Ala Ser Met Lys Arg Lys
                                     280
                275
Gly Val Glu Leu Lys Asp Ile Lys Arg Cys Leu Gly Tyr His Leu
                290
                                     295
Asp Val Ser Leu Ala Phe Ser Glu Ile Ser Val Gly Ala Glu Phe
                305
                                     310
Asn Lys Asp Asp Cys Val Lys Arg Gly Glu Gly Arg Ala Val Asn
                320
                                     325
Ile Thr Ser Glu Asn Leu Ile Asp Asp Val Val Ser Leu Ile Arg
                335
Gly Gly Thr Arg Lys Tyr Ala Phe Glu Leu Lys Glu Lys Leu Leu
                                     355
                350
Arg Gly Thr Val Ile Asp Val Thr Asp Phe Val Asn Arg Ala Ser
                                     370
                                                          375
                365
Ser Ile Asn Asp Ala Pro Val Leu Ile Ser Gln Lys Leu Ser Pro
                                                          390
                380
                                     385
Ile Tyr Asn Leu Val Pro Val Lys Met Lys Asn Ala His Leu Lys
                                     400
                395
Lys Gln Asn Leu Glu Arg Ala Ile Glu Asp Tyr Ile Asn Glu Phe
                                                          420
                 410
                                     415
Ser Val Arg Lys Cys His Thr Cys Gln Asn Gly Gly Thr Val Ile
                                     430
                 425
Leu Met Asp Gly Lys Cys Leu Cys Ala Cys Pro Phe Lys Phe Glu
                                     445
                                                          450
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Gly Ile Ala Cys Glu Ile Ser Lys Gln Lys Ile Ser Glu Gly Leu
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Pro Ala Leu Glu Phe Pro Asn Glu Lys
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 Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
                                      25
 Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu
                                       40
                  35
 Asn Gly Ile Asn Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
                                       55
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser
                                       70
                  65
 Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
                                       85
                  80
 Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys
                                                          105
                                      100
                  95
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Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg
                                    115
                110
Trp Ile Thr Phe Trp Gln Ser Ile Ile Ser Thr Leu Thr
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Met Ala Arg Gly Ala Ala Leu Ala Leu Leu Leu Phe Gly Leu Leu
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Gly Val Leu Val Ala Ala Pro Asp Gly Gly Phe Asp Leu Ser Asp
                                      25
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Ala Leu Pro Asp Asn Glu Asn Lys Lys Pro Thr Ala Ile Pro Lys
                                                           45
                 35
                                      40
Lys Pro Ser Ala Gly Asp Asp Phe Asp Leu Gly Asp Ala Val Val
                                                          60
                                      55
                 50
Asp Gly Glu Asn Asp Asp Pro Arg Pro Pro Asn Pro Pro Lys Pro
                                      70
                 65
Met Pro Asn Pro Asn Pro Asn His Pro Ser Ser Ser Gly Ser Phe
                 80
                                      85
Ser Asp Ala Asp Leu Ala Asp Gly Val Ser Gly Gly Glu Gly Lys
                                     100
                                                          105
                 95
Gly Gly Ser Asp Gly Gly Gly Ser His Arg Lys Glu Gly Glu Glu
                110
                                     115
                                                          120
Ala Asp Ala Pro Gly Val Ile Pro Gly Ile Val Gly Ala Val Val
                125
                                     130
                                                         135
Val Ala Val Ala Gly Ala Ile Ser Ser Phe Ile Ala Tyr Gln Lys
                140
                                     145
Lys Lys Leu Cys Phe Lys Glu Asn Gly Gln Leu Ala Gly Ser Leu
                155
                                     160
Gly Pro Cys Ile Arg Ile Arg Arg Glu Ala Gly Asn Arg Thr Arg
                170
                                     175
Gly Gly Gly His Gly Glu Pro Pro Glu Cys Gln Arg Arg Ala Ser
                                     190
                                                          195
                185
Cys Ser Ala Tyr Ser Phe Arg Glu Ile Glu Asp Cys Arg Gln Lys
                                     205
                200
Gln Pro Arg Arg Trp Gln Gln Gly
                215
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Met Val Ile Ala Phe Trp Lys Val Phe Leu Ile Leu Ser Cys Leu
Ala Gly Gln Val Ser Val Val Gln Val Thr Ile Pro Asp Gly Phe
                                                           30
                  20
                                      25
Val Asn Val Thr Val Gly Ser Asn Val Thr Leu Ile Cys Ile Tyr
                                      40
                 35
Thr Thr Val Ala Ser Arg Glu Gln Leu Ser Ile Gln Trp Ser
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55

60

50

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Phe Phe His Lys Lys Glu Met Glu Pro Ile Ser Ile Tyr Phe Ser
                 65
                                     70
Gln Gly Gly Gln Ala Val Ala Ile Gly Gln Phe Lys Asp Arg Ile
                                     85
                 80
Thr Gly Ser Asn Asp Pro Val Lys Pro Ser Lys Pro Leu Cys Ser
                                    100
                 95
Val Gln Gly Arg Pro Glu Thr Gly His Thr Ile Ser Leu Ser Cys
                110
                                    115
                                                         120
Leu Ser Ala Leu Gly Thr Pro Ser Pro Val Tyr Tyr Trp His Lys
                                    130
                125
                                                         135
Leu Glu Gly Arg Asp Ile Val Pro Val Lys Glu Asn Phe Asn Pro
                140
                                    145
Thr Thr Gly Ile Leu Val Ile Gly Asn Leu Thr Asn Phe Glu Gln
                155
                                    160
Gly Tyr Tyr Gln Cys Thr Ala Ile Asn Arg Leu Gly Asn Ser Ser
                                    175
                170
Cys Glu Ile Asp Leu Thr Ser Ser His Pro Glu Val Gly Ile Ile
                                    190
Val Gly Ala Leu Ile Gly Ser Leu Val Gly Ala Ala Ile Ile Ile
                                    205
                200
Ser Val Val Cys Phe Ala Arg Asn Lys Ala Lys Ala Lys Ala Lys
                                    220
                215
Glu Arg Asn Ser Lys Thr Ile Ala Glu Leu Glu Pro Met Thr Lys
                230
                                    235
                                                         240
Ile Asn Pro Arg Gly Glu Ser Glu Ala Met Pro Arg Glu Asp Ala
                245
                                    250
Thr Gln Leu Glu Val Thr Leu Pro Ser Ser Ile His Glu Thr Gly
                                                         270
                260
                                    265
Pro Asp Thr Ile Gln Glu Pro Asp Tyr Glu Pro Lys Pro Thr Gln
                275
                                    280
                                                         285
Glu Pro Ala Pro Glu Pro Ala Pro Gly Ser Glu Pro Met Ala Val
                290
                                    295
Pro Asp Leu Asp Ile Glu Leu Glu Leu Glu Pro Glu Thr Gln Ser
                                                         315
                305
                                    310
Glu Leu Glu Pro Glu Pro Glu Pro Glu Pro Glu Ser Glu Pro Gly
                                    325
                320
Val Val Val Glu Pro Leu Ser Glu Asp Glu Lys Gly Val Val Lys
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                                    340
                                                         345
Ala ·
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Gln Ser Gly Val Ala Pro Lys Ala Val Leu Leu Asp Pro Pro
Trp Ser Thr Ala Phe Lys Gly Glu Lys Val Ala Leu Ile Cys Ser
                 35
                                      40
Ser Ile Ser His Ser Leu Ala Gln Gly Asp Thr Tyr Trp Tyr His
                                      55
Asp Glu Lys Leu Leu Lys Ile Lys His Asp Lys Ile Gln Ile Thr
                 65
                                      70
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Glu Pro Gly Asn Tyr Gln Cys Lys Thr Arg Gly Ser Ser Leu Ser

```
80
                                     85
Asp Ala Val His Val Glu Phe Ser Pro Asp Trp Leu Ile Leu Gln
                 95
                                    100
Ala Leu His Pro Val Phe Glu Gly Asp Asn Val Ile Leu Arg Cys
                                    115
                110
                                                         120
Gln Gly Lys Asp Asn Lys Asn Thr His Gln Lys Val Tyr Tyr Lys
                                    130
                125
                                                         135
Asp Gly Lys Gln Leu Pro Asn Ser Tyr Asn Leu Glu Lys Ile Thr
                140
                                    145
Val Asn Ser Val Ser Arg Asp Asn Ser Lys Tyr His Cys Thr Ala
                155
                                    160
                                                         165
Tyr Arg Lys Phe Tyr Ile Leu Asp Ile Glu Val Thr Ser Lys Pro
                170
                                    175
Leu Asn Ile Gln Val Gln Glu Ile Ala Arg Pro Ser Asp Trp Ala
                185
                                    190
Gly Ala Gly Pro Pro Asp Ser Arg Ser Leu Pro Cys Gly Leu Lys
                200
                                    205
Thr Gln Gly Leu Thr Gly Val Arg Trp Arg Gln
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Gly Asn Thr Asp Gly Leu Lys Glu Pro Leu Ser Phe His Val Thr
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Trp Ile Ala Ser Phe Tyr Asn His Ser Trp Lys Gln Asn Leu Val
                 35
                                     40
Ser Gly Trp Leu Ser Asp Leu Gln Thr His Thr Trp Asp Ser Asn
                                      55
Ser Ser Thr Ile Val Phe Leu Cys Pro Trp Ser Arg Gly Asn Phe
                                      70
                 65
Ser Asn Glu Glu Trp Lys Glu Leu Glu Thr Leu Phe Arg Ile Arg
                 80
                                     85
Thr Ile Arg Ser Phe Glu Gly Ile Arg Arg Tyr Ala His Glu Leu
                 95
                                     100
Gln Phe Glu Tyr Pro Phe Glu Ile Gln Val Thr Gly Gly Cys Glu
                110
                                     115
                                                         120
Leu His Ser Gly Lys Val Ser Gly Ser Phe Leu Gln Leu Ala Tyr
                125
                                     130
                                                         135
Gln Gly Ser Asp Phe Val Ser Phe Gln Asn Asn Ser Trp Leu Pro
                                    145
                140
Tyr Pro Val Ala Gly Asn Met Ala Lys His Phe Cys Lys Val Leu
                155
                                     160
Asn Gln Asn Gln His Glu Asn Asp Ile Thr His Asn Leu Leu Ser
                170
                                    175
Asp Thr Cys Pro Arg Phe Ile Leu Gly Leu Leu Asp Ala Gly Lys
                185
                                     190
                                                         195
Ala His Leu Gln Arg Gln Val Lys Pro Glu Ala Trp Leu Ser His
                200
                                     205
Gly Pro Ser Pro Gly Pro Gly His Leu Gln Leu Val Cys His Val
                215
                                     220
Ser Gly Phe Tyr Pro Lys Pro Val Trp Val Met Trp Met Arg Gly
                230
                                     235
Glu Gln Glu Gln Gly Thr Gln Arg Gly Asp Ile Leu Pro Ser
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250
                245
Ala Asp Gly Thr Trp Tyr Leu Arg Ala Thr Leu Glu Val Ala Ala
                                    265
                260
Gly Glu Ala Ala Asp Leu Ser Cys Arg Val Lys His Ser Ser Leu
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Glu Gly Gln Asp Ile Val Leu Tyr Trp Gly Leu Ala Leu Trp Phe
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                                    295
Arg Lys Arg Cys Phe Cys
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Phe Leu Leu Pro Gly Ser Leu Gly Ala Glu Ser His Leu Ser Leu
                 20
                                      25
Leu Tyr His Leu Thr Ala Val Ser Ser Pro Ala Pro Gly Thr Pro
                 35
                                      40
Ala Phe Trp Val Ser Gly Trp Leu Gly Pro Gln Gln Tyr Leu Ser
                 50
                                      55
Tyr Asn Ser Leu Arg Gly Glu Ala Glu Pro Cys Gly Ala Trp Val
                                      70
                 65
Trp Glu Asn Gln Val Ser Trp Tyr Trp Glu Lys Glu Thr Thr Asp
                 80
                                      85
Leu Arg Ile Lys Glu Lys Leu Phe Leu Glu Ala Phe Lys Ala Leu
                 95
                                     100
Gly Gly Lys Gly Pro Tyr Thr Leu Gln Gly Leu Leu Gly Cys Glu
                110
                                    115
Leu Gly Pro Asp Asn Thr Ser Val Pro Thr Ala Lys Phe Ala Leu
                125
                                     130
Asn Gly Glu Glu Phe Met Asn Phe Asp Leu Lys Gln Gly Thr Trp
                140
                                     145
Gly Gly Asp Trp Pro Glu Ala Leu Ala Ile Ser Gln Arg Trp Gln
                155
                                     160
Gln Gln Asp Lys Ala Ala Asn Lys Glu Leu Thr Phe Leu Leu Phe
                170
                                     175
Ser Cys Pro His Arg Leu Arg Glu Hi's Leu Glu Arg Gly Arg Gly
                185
                                     190
                                                         195
Asn Leu Glu Trp Lys Glu Pro Pro Ser Met Arg Leu Lys Ala Arg
                200
                                     205
Pro Ser Ser Pro Gly Phe Ser Val Leu Thr Cys Ser Ala Phe Ser
                215
                                     220
                                                         225
Phe Tyr Pro Pro Glu Leu Gln Leu Arg Phe Leu Arg Asn Gly Leu
                230
                                     235
                                                         240
Ala Ala Gly Thr Gly Gln Gly Asp Phe Gly Pro Asn Ser Asp Gly
                245
                                     250
                                                         255
Ser Phe His Ala Ser Ser Ser Leu Thr Val Lys Ser Gly Asp Glu
                260
                                     265
His His Tyr Cys Cys Ile Val Gln His Ala Gly Leu Ala Gln Pro
                275
                                     280
Leu Arg Val Glu Leu Ala Pro Trp Ile Ser Leu Arg Gly Asp Asp
                290
                                     295
Thr Gly Val Leu Leu Pro Thr Pro Gly Glu Ala Gln Asp Ala Asp
                305
Leu Lys Asp Val Asn Val Ile Pro Ala Thr Ala
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320 325

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Leu Tyr Ser Asp Ala Asn Ile Tyr Cys Gln Ile Asp His Lys Ala

Asp Val Val Ser

115

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Leu Ala Glu Asn Ser Asp Asp Tyr Asp Leu Met Tyr Val Asn Leu
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                                      25
Asp Asn Glu Ile Asp Asn Gly Leu His Pro Thr Glu Asp Arg Cys
                                      40
                                                           45
Glu Thr Ala Ile Leu Phe Pro Met Arg Ser Lys Lys Ile Phe Gly
                 50
                                      55
                                                           60
Ser Val His Pro Val Arg Pro Met Arg Leu Glu Ser Phe Ser Ala
                 65
                                      70
Cys Ile Trp Val Lys Ala Thr Asp Val Leu Asn Lys Thr Ile Leu
                 80
                                      85
Phe Ser Tyr Gly Thr Lys Arg Asn Pro Tyr Glu Ile Gln Leu Tyr
                 95
                                     100
                                                          105
Leu Ser Tyr Gln Ser Ile Val Phe Val Val Gly Gly Glu Glu Asn
                110
                                     115
                                                          120
Lys Leu Val Ala Glu Ala Met Val Ser Leu Gly Arg Trp Thr His
                125
                                     130
                                                          135
Leu Cys Gly Thr Trp Asn Ser Glu Glu Gly Leu Thr Ser Leu Trp
                140
                                     145
                                                          150
Val Asn Gly Glu Leu Ala Ala Thr Thr Val Glu Met Ala Thr Gly
                155
                                     160
                                                          165
His Ile Val Pro Glu Gly Gly Ile Leu Gln Ile Gly Gln Glu Lys
                170
                                     175
                                                          180
Asn Gly Cys Cys Val Gly Gly Gly Phe Asp Glu Thr Leu Ala Phe
                185
                                     190
Ser Gly Arg Leu Thr Gly Phe Asn Ile Trp Asp Ser Val Leu Ser
                200
                                     205
Asn Glu Glu Ile Arg Glu Thr Gly Gly Ala Glu Ser Cys His Ile
                215
                                     220
Arg Gly Asn Ile Val Gly Trp Gly Val Thr Glu Ile Gln Pro His
                230
                                     235
Gly Gly Ala Gln Tyr Val Ser
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Phe Leu Pro Phe Cys Leu Cys Gln Asp Glu Tyr Met Glu Ser Pro
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Gln Thr Gly Gly Leu Pro Pro Asp Cys Ser Lys Cys Cys His Gly
                 35
                                                           45
                                      40
Asp Tyr Ser Phe Arg Gly Tyr Gln Gly Pro Pro Gly Pro Pro Gly
                 50
                                      55
                                                           60
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Pro Pro Gly Ile Pro Gly Asn His Gly Asn Asn Gly Asn Asn Gly
                65
                                     70
                                                         75
Ala Thr Gly His Glu Gly Ala Lys Asp Cys Ile His Gly Phe Ser
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                                                         90
Gly Asn Pro Leu Gln Gln Ser Glu Gln Trp Asp Tyr Leu Gln Gln
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Cys
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